

Low platelet counts in acute lymphoblastic leukemia: frequency and correlates

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ABSTRACT

Introduction: Acute Lymphoblastic Leukemia (ALL) is a common hematological malignancy of children, and various classifications are of help in diagnosis, management, treatment, prognosis, and outcome. Among other hematological manifestations, a frequent observation is the presence of anemia and thrombocytopenia in a sizeable number of cases; some authors have postulated various mechanisms to account for this finding, and related their presence with initial classification and final outcome of the disease.

Objective: To assess the frequency and factors related to low platelet count among patients diagnosed with acute lymphoblastic leukemia at oncology department of a tertiary care hospital of Peshawar, Khyber Pakhtunkhwa.

Materials & Methods: A cross sectional descriptive study was conducted at Oncology Department, Hayatabad Medical Complex (HMC), Peshawar, Khyber Pakhtunkhwa, for twelve months, from August 2018 to July 2019, on patients diagnosed with acute lymphoblastic leukemia. Thrombocytopenia was defined as platelet count of $<150,000/\mu\text{l}$ and platelet count was performed soon after the exact diagnosis of acute lymphoblastic leukemia was made. Age, gender, presence of anemia and deranged liver function tests were correlated with low platelet count. SPSS 24.0 was used for descriptive statistics and binary logistic regression, keeping $p \leq 0.05$ significant.

Results: A total of 90 patients diagnosed as acute lymphoblastic leukemia were included in the study. Mean age of the patients was 15.43 ± 4.756 years; 64(71.1%) were male while 26(28.9%) patients were female. Low platelet count was observed in 41(45.5%) patients while 49(54.5%) had platelet count within the normal range. Low hemoglobin levels were strongly related to presence of low platelet count in our sample ($p < 0.001$).

Conclusion: Low platelet count was a common finding at the time of diagnosis among patients diagnosed with acute lymphoblastic leukemia. Presence of anemia was statistically significantly correlated with presence of low platelet count among these patients at the time of diagnosis of this hematological malignancy.

Keywords: Leukemia, Lymphoblastic, Acute; Diagnosis; Platelet Count; Thrombocytopenia; Anemia.

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INTRODUCTION

Hematological malignancies have been diagnosed at much high frequency in last two decades as compared to remote past because of advancements in diagnostic procedures.¹ These malignancies are basically a diverse group of disorders with wide range of symptoms, management plans and prognostic factors.² Almost all age groups have been affected by leukemias or lymphomas but younger age group has been mostly affected by Acute Lymphoblastic Leukemia (ALL) as compared to older age group.³

Normal hematological parameters are necessary for overall homeostasis of the human body. Platelets are one of the most important components of human blood and play the main role in hemostasis on exposure to trauma and other conditions of injury to the body.⁴ A lot of hematological malignancies may involve this cell line directly or indirectly.⁵ Malignancies which indirectly involve platelets warrant more careful eye of the treating physician in order to pick this abnormality in time and manage it to avoid further complications.⁶

Studies have been performed around the globe regarding low platelet count in ALL either at time of diagnosis or with response to standard treatment offered for this condition. Jaime-Pérez et al⁷ in 2019 published their data of 10-year experience of their department at a Mexican hospital, concluding that anemia and thrombocytopenia at time of diagnosis were found in 83% of the cases, leukocytosis in 36.6% and leucopenia in 36.1% of cases.⁷ Zeidler et al,⁸ in 2012, studied the same phenomenon in patients of ALL but not at the time of diagnosis, rather evaluated low platelet count after induction therapy and revealed that platelet counts after induction treatment may improve treatment stratification for patients with childhood ALL and be of particular interest in non-minimal residual disease-based trials.⁸ Yenicesu et al,⁹ in 2000, looked for the presence of Idiopathic Thrombocytopenic Purpura (ITP) in ALL and came up with the findings that though rare, but this phenomenon cannot be completely ruled out among patients suffering from ALL and may be one of the important causes of low platelet counts among these patients.⁹

Hematological malignancies have been commonly encountered malignancies in our part of the world and pose a great burden on our health care budget. Leukemias, if complicated with other problems, may lead to increased mortality and morbidity and make things complex both for the patient and treating team. Sultan et al,¹⁰ in 2016, published findings of adult ALL and summarized that low platelet count was a common finding among these patients.¹⁰ Limited local data are available of low platelet count among patients of all age group at diagnosis of ALL. This study was planned with the rationale to look for the frequency and factors related to low platelet count among patients diagnosed with acute lymphoblastic leukemia in our center.

MATERIALS & METHODS

This cross sectional study was conducted at the Oncology Department, Hayatabad Medical Complex (HMC), Peshawar, from August 2018 to July 2019. All patients of ALL diagnosed by consultant oncologist/hematologist on basis of National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines¹¹ were included in this study using non probability consecutive sampling technique. Sample size was calculated by WHO sample size calculator using population prevalence of cytopenia in ALL as 6%.¹² Inclusion criteria included patients between the age of 1 and 25 years diagnosed with ALL waiting for induction therapy. Patients who had already been put on treatment were excluded from the study. Exclusion criteria also included other malignancies, autoimmune disorders, chronic liver disease, and pregnant women. Patients with unclear diagnosis or suspicion of other causes leading to low platelet count were also excluded from the study.

After approval from the ethical review board and written informed consent from patients or their care-givers, patients fulfilling the above mentioned inclusion and exclusion criteria were included in the study. The diagnosis of thrombocytopenia was made with platelet count of less than 150,000/ μ l which was performed soon after the diagnosis of acute lymphoblastic leukemia was made.¹³ Anemia was described as blood hemoglobin values of <11 g/dl.¹⁴ Deranged liver function test meant either of liver enzymes or bilirubin levels more than normal range.¹⁵ Age, gender, presence of anemia and deranged liver function tests were correlated with low platelet count in our study population.

Characteristics of patients and the distribution of platelet counts were described by using descriptive statistics. Participants were

categorized for comparison by presence or absence of low platelet count. Chi-square test was used to determine between-group variances in categorical correlates. Binary logistic regression analysis was done to evaluate the relationship of age, gender, presence of anemia, and deranged liver function tests with low platelet count in our subjects. All statistical analysis was performed using Statistics Package for Social Sciences version 24.0 (SPSS 24.0). Differences between groups were considered significant if p value was ≤ 0.05 .

RESULTS

A total of 90 patients diagnosed as acute lymphoblastic leukemia at our department during the study period were included in analysis. Mean age of the patients was 15.43 ± 4.756 years; 64(71.1%) were male and 26(28.9%) were female. Low platelet count was observed in 41(45.5%) patients while 49 (54.5%) had platelet count within the normal range. Pearson chi-square analysis (Table I) showed that Low hemoglobin levels were strongly related to presence of low platelet count in our target population (p-value<0.001).

Table 1: Socio-demographic data and platelet counts of patients with Acute Lymphoblastic Leukemia (n=90).

Socio-demographic factors	Platelet counts (mm ³)		p value
	Normal f (%)	Low f (%)	
Age Groups			
12 year or less	24 (48.9)	14 (34.1)	0.154
>12 years	25 (51.1)	27 (65.9)	
Gender			
Male	37 (75.5)	27 (65.8)	0.315
Female	12 (24.5)	14 (34.2)	
Deranged liver functions			
No	24 (48.9)	17 (41.5)	0.475
Yes	25 (51.1)	24 (58.5)	
Presence of anemia			
No	38 (77.5)	15 (36.6)	<0.001
Yes	11 (22.5)	26 (63.4)	

Table 2 shows that binary logistic regression analysis confirmed this association and patients with low levels of hemoglobin had clearly more chances of having low platelet count as well [(p<0.001, OR with 95% CI-6.227 (2.402-16.142)].

Table 2: Factors correlating with low platelet count among patients by the binary logistic regression (n=90).

Correlated Factors	p value	OR (95% CI)
Age (reference value is <12 years)	0.315	1.659 (0.619-4.447)
Gender (reference value is male)	0.515	0.698 (0.237-2.058)
Deranged Liver functions (reference value is normal liver functions)	0.266	1.722 (0.661-4.486)
Presence of anemia (reference value is no anemia)	<0.001	6.227 (2.402-16.142)

DISCUSSION

Cancers are one of the leading causes of morbidity and mortality among all age groups all around the world.¹ Malignancies related to hematopoietic system have been no exception to it. Lymphoid

and other cell lines get grossly affected in such conditions.² Usually, the type of cell line reflects the exact nature of underlying malignancy, but more than one type of cells may be affected directly or indirectly in these disorders. Acute lymphoblastic leukemia usually involves unchecked proliferation

of white blood cells which is main pathological finding in this condition, but this is not the only finding.³ Variety of laboratory and clinical findings may be part of spectrum of acute lymphoblastic leukemia. This study was planned with the rationale to assess the frequency and factors related to low platelet count among patients diagnosed with acute lymphoblastic leukemia at oncology department of a tertiary care hospital.

Jawaid et al,¹⁶ investigated hematological causes of thrombocytopenia in children at Aga Khan University Hospital, Karachi. They concluded that hematological malignancies were one of the commonest causes of low platelet count in the age group they studied. It was observed in their study that acute lymphoblastic leukemia was the commonest cause of hematological thrombocytopenia followed by idiopathic thrombocytopenic purpura and aplastic anemia. Our study supported their findings and around 40% of patients diagnosed with ALL in our study had low platelet counts.

Strauss et al¹⁷ published an interesting study in 2011 regarding evaluation of immature platelet count in distinguishing thrombocytopenia in pediatric acute lymphocytic leukemia from immune thrombocytopenia. They found that children diagnosed with acute lymphocytic leukemia (ALL) had considerably elevated immature platelet fraction (median 10%, $p < 0.01$), suggesting that thrombopoiesis is stimulated despite virtual absence of bone marrow progenitors. We did not study immature platelet count or included patients of ITP but found that low platelet count was a consistent finding among patients of ALL.

An interesting study published by Hara et al,¹⁸ long ago in 1990, look at the same phenomenon from another perspective. Considering the high prevalence of thrombocytopenia in patients with hematological malignancies, they tried to establish the presentation of acute leukemia with normal platelet count at diagnosis. They concluded that 36(17.8%) of 202 children with acute lymphoblastic leukemia (ALL) and 02(03.7%) of 54

children with acute non-lymphoblastic leukemia (ANLL) had a platelet count over $150 \times 10^9/l$ at diagnosis which shows that most of the patients had low platelet count at time of diagnosis. Male and anemic patients had more chances of having thrombocytopenia as compared to females and patients with normal hemoglobin levels. Our findings supported their results in general as 41% of our patients had low platelets and presence of anemia was a strong predictor of low platelet count in our study population.

Kakaje et al,¹⁹ published a study in 2020 from Syria concluding that most patients diagnosed with ALL had either abnormal platelet count (89.3%) or low hemoglobin level (88.8%) when presenting, with only 2.0% having normal levels for both. They suggested that having normal hemoglobin and platelet count can be used for quick screening in crisis time like in Syria for prioritizing the patients. Both the parameters they found deranged in their study participants were also found abnormal in our study subjects highlighting that anemia and low platelet count should not be missed before starting treatment of ALL.

LIMITATION

The major limitation of our study is the lack of generalizability as patients from a single center were included in the study. The sample size, and design of study pose methodological issues as well. Patients were not evaluated before the diagnosis of ALL to look for baseline platelet count of study participants. Future studies with better design may generate better and generalizable results.

CONCLUSION

Low platelet count was a common finding at the time of diagnosis among patients diagnosed with acute lymphoblastic leukemia. Presence of anemia was statistically significantly correlated with presence of low platelet count among these patients at the time of diagnosis of this hematological malignancy.

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